Remarks

Applicants thank the Examiner for the helpful telephone conference, and here elect with traverse claims 28-32 and 61, as here amended, of Group 20, directed to a composition comprising a synthetic peptide of SEQ ID NO: 93, class 530, subclass 300. For search purposes of claim 30, Applicants further elect the species having Valine (V). In the event that method claims relating to the compositions are rejoined, applicants elect for search purposes of claim 50 the species of Multiple Sclerosis.

Applicants here traverse restriction of the claims into 76 groups, and request reconsideration of this restriction in view of the following remarks. Further, Applicants here amend the claims, and believe that claims as here amended address both election of a restriction group and a species, in the event that the Examiner rejoins one or more groups of claims. Applicants acknowledge that in the event that a broad claim is allowed, that the examiner may search and allow additional species which can be to the allowed claim.

The claims as originally filed address a single problem and provide a single solution. The problem is the need for compositions and methods for treating autoimmune diseases in a subject, specifically, treating demyelinating conditions such as multiple sclerosis (MS). There is no cure for MS, which is ultimately fatal (see Specification on page 2, lines 9-10), and current treatments, while providing relief by decreasing somewhat severity and frequency of MS episodes, do not eliminate episodes.

A general problem existing in medicine is treatment of autoimmune diseases, *viz.*, providing optimal specific treatment such that ability of the subject to fight infectious disease and carry out the steps of immune surveillance necessary to prevent a transformed cell from developing into a tumor are not negatively affected. Inhibiting general function of the immune system, as in subjects treated with agents such as rapamycin or FK506, or in patients infected with HIV who lack sufficient T cells, is not optimal for these reasons. Instead, treatment of an autoimmune disease such as MS is optimally accomplished by inhibiting interaction of the particular autoantigen with cells that are involved in the first step of the pathology, i.e., the first step for recognition of the autoantigen that induces a pathway of immune attack and inflammatory responses, for example, induces secretion of cytokines of inflammation.

The claims share a special technical feature, based on the discovery that the peptides of the claims as here amended share particular amino acid sequences as to be largely identical or homologous. The sequences have functional residues that differ at each of only a few positions, however the differences involve functionally similar amino acid residues. Peptides herein also satisfy functional criteria, as determined by data obtained by in vitro chemical assays and cell-based assays provided in the Figures of the Specification as filed. Further, the methods and compositions of claims as originally filed employ the same special technical feature: claims are directed to synthetic peptides having a particular similar core sequence of amino acids, and to their identification and use for treatment of demyelinating conditions, notably MS. The compositions claimed herein function by competing with an autoantigen for binding to MCH class II proteins on a cell.

Thus claim 28, as here amended, is directed to peptides that share functional and structural features: all have a large bulky hydrophobic amino acid in the amino acid position "P1", corresponding to a location in the class II MHC protein binding surface identified as the "P1 pocket", which is defined in the specification on page 11, lines 12-25. Further, each has a bulky hydrophobic group at "P4", also defined in the Specification. Most of the amino acids of these peptides are identical at all other positions. A proline residue (P) is present in some otherwise identical sequences, as is a variation of a peptide having the desired activities, and as explained in the Application as filed to reduce peptidase digestion of these sequences in vivo.

Applicants assert that the compositions of claim 28 as here amended, which are structurally and functionally related peptides that were obtained by design and produced by organic synthetic methods, are more appropriately treated as chemical variants of a core organic molecule, as are the numerous compositions in classical drug patents such as U.S. serial numbers 5,360,800, 5,811,426; or more recently, 6,706,737 B2.

Applicants assert that the peptides that are designed by the methods of the specification as filed are not obtained from nature, i.e., none of the amino acid sequences of the peptides in the claims as filed is found in the genome of any organism. For at least that reason, the peptides of the claims as here amended should be considered as a group of synthetic compounds.

Further, claim 28 is here amended to delete from that claim the peptides that are less related to each other by amino acid sequence. This claim is further amended to delete peptides

that were designed as tests of the functional requirements for amino acids that are located at important positions, i.e., this claim is further amended to delete "control" peptide sequences. This amendment has been made to advance prosecution of the claims, and Applicants reserve the right to pursue the deleted subject matter in the present application or another application sharing the filing date and/or priority date of the present application.

Many advantages of the compositions and methods are presented in the Specification. The advantages include greater efficacy in an assay using a standard reagent (the peptide MBP 85-99; SEQ ID NO: 1), when compared to Copaxone (or Cop 1), which is an FDA approved pharmaceutical agent for MS. See claim 36 as originally filed.

Further, the various different peptide compositions of the claims as originally filed can be used therapeutically in a single pharmaceutical composition together (even linked together into the same hetero-oligomeric peptide; see claim 19 as originally filed), or can be used therapeutically with another therapeutic agent which is a random heteropolymer such Copaxone (see claim 7 as originally filed).

The application describes methods of obtaining such peptides (claims 34-48), and methods of using such peptides, i.e., for treating a subject (claims 49-58). To advance prosecution and not to concede the propriety of the restriction, applicants here cancel the claims 34-48. Further, claim 49 is here amended to delete peptides having amino acid sequence that are less structurally related as a group, and to conform to claim 28 as here amended.

The peptides of the present application present regulatory and commercial advantages over current therapeutic agents for treatment of MS. Unlike Copaxone, which comprises amino acid copolymers that are chemically random in amino acid sequence and of variable in length, the peptides of the present claims are uniform in sequence and length, which are features that characterize a more acceptable therapeutic molecule from a regulatory point of view.

Further, unlike biological agents such as β-interferon that are used in treatment of demyelinating conditions, the compositions of the claims are not biological effectors that are found in small amounts in a subject, implying that increasing the dose may result in undesirable side effects.

Further unlike β-interferon, the molecules of the present invention are produced by chemical synthesis, and are thereby free of undesirable cell culture contaminants such as

bacteria, viruses, and prions (not mere theoretical considerations in view of recent influenza vaccine being contaminated with bacteria and therefore unusable.)

It appears that the Examiner has identified each restriction group on the basis of each independent claim and each peptide sequence, rather than considering the shared functional and structural technical features of the peptides. Separation of the claims into 76 groups is inapposite both to the nature of the invention and to the technical problem to be solved.

Applicants here elect claims directed to a novel composition. Further, Applicants respectfully request rejoinder of the compositions in claim 28 as here amended to the elected composition, into a single restriction group.

Additionally or alternatively in the event that only one sequence is to be searched, Applicants respectfully request that methods of use of the compositions for treating a demyelinating condition be rejoined to the corresponding composition group, as consideration of the method dependent on that sequence would not present a considerable additional burden.

The steps in the various methods of identification of peptides do not, as asserted by the Restriction Requirement, provide evidence of differences in methods of action of the different compositions, rather are merely different assays of known downstream steps in an immune response that can be altered in response to the presence of the inhibiting peptide due to the initial presence (or amount, compared to the absence) of the peptide. Each of the different assays used as a method of identification of the activities of the peptides, may be considered for restriction analysis an exemplary species of the methods herein.

There is simply no evidence presented that the different compositions having different amino acid sequences act at different steps in treating the demyelinating condition, or act on different molecular targets.

This unity of action of the different peptides, as the Examiner will appreciate, bears on authority to require restriction is defined and limited by statute (35 U.S.C. § 121, first sentence) as follows:

> If two or more <u>independent and distinct</u> inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions. (emphasis added)

The implementing regulations of the Patent and Trademark Office include the mandate that restriction is appropriate only in cases having inventions that are both independent and distinct, 37 C.F.R. §§ 1.141-142.

Without any evidence that the different peptides act at different steps or on different targets, there is no showing of independence and distinctness of the method claims. Applicants assert that the claims directed to methods in the present application which have been grouped separately by the Examiner, are in fact not "independent and distinct" so as to justify the restriction requirement.

However to advance prosecution, method claims 33-48 are here canceled. Applicants have thereby cancel broad functional method claims directed to identifying such peptides and to preparing pharmaceutical compositions, and reserve the right to pursue the subject matter of those claims in this application, or in another application sharing the filing date and/or the priority data of this application.

The Examiner in the Office Action referenced different subclasses of the Patent and Trademark Office classification system in which some of the 76 groups of claims would allegedly be classified. This basis fails to justify the restriction requirement in this application. Notably, most of the alleged separate inventions have the same classification, i.e., class 530 for Groups 1-26 (claims 1-32, 55-56 and 59-61) and class 435 for Groups 50-53 (claims 34-48). *Prima facie*, therefore, there should be no necessity for non-coextensive literature searches in relation to the methods and compositions of the pending claims for each of two groups of claims, 1-26 and 34-48.

Moreover, Applicants respectfully assert that classification of the groups of claims does not establish independence and distinctness of these groups of claims. The classification system has no statutory recognition as evidence of whether inventions are independent and distinct, but is merely an aid searching for patents. Accordingly, the classification system is unreliable for requiring restriction between claims to the various aspects of Applicants' unitary invention.

The classification system is also an unreliable basis for requiring restriction between claims to the various embodiments of Applicants' unitary invention, because the system exhibits considerable overlap in technical definitions. In particular, the definitions of subclasses in the classification system do not prevent the Examiner from assessing patentability of claims of one

claim group, on the basis of patent references found in subclass(es) with which the Examiner has associated another group of claims.

Accordingly, based at least on the shared special technical feature, Groups 4-26 directed to compositions having amino acid sequences, are clearly interrelated and interdependent, and not "independent and distinct." Applicants point out that groups 27-49, encompassing claims 33, 49-54 and 57-58 directed to methods of reducing demyelination in a subject, have only one use envisioned in the specification as filed: treating a subject for MS.

An alternative suggested by the Restriction Requirement, use of the peptides for eliciting production of antibodies, is neither envisioned nor claimed in the present application. Further, Applicants assert that while this use is formally possible, it is a mere constructive alternative, as one of ordinary skill in the art of autoimmune disease recognizes its greatly decreased medical and commercial importance compared with reducing demyelination in a subject having MS.

The courts have stated that applicants are permitted to claim several aspects of their invention in one application, as the Applicants have done herein. For example, the court in In re Kuehl, 456 F.2d 658, 666; 117 U.S.P.Q. 250, 256 (CCPA 1973), has stated:

> We believe the constitutional purpose of the patent system is promoted by encouraging applicants to claim, and therefore to describe in the manner required by 35 U.S.C. § 112 all aspects as to what they regard as their invention, regardless of the number of statutory classes involved.

This interest is consistent with the practical reality that a sufficiently detailed disclosure supporting claims to one aspect of an invention customarily is sufficient to support claims in the same application to other aspects of the invention. In addition, Applicants respectfully suggest that in view of the continued increase in official fees and the potential limitation of an applicants.

In addition, Applicants respectfully suggest that in view of the continued increase in official fees and the potential limitation of an applicant's financial resources, an action which imposes a 76-way restriction requirement can be prohibitive, to a non-profit entity such as an academic institution, and thereby contravene the constitutional purpose to promote and encourage the progress of science and the useful arts.

Accordingly, to protect a patentee's rights and to serve the public's interest in the patenting of therapeutic agents, Applicants respectfully urge the Examiner not to require so substantial a number of restriction groups in the present application where various aspects of a unitary invention are claimed.

For the foregoing reasons and in view of the present amendment to the claims, it is respectfully urged that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims. If however the Examiner does not entirely eliminate the restriction, Applicants urge that fewer groups of claims be considered, and suggest such groupings, as also mentioned above.

Upon entry of the present amendment, groups 1, 2, 3 (in part), 4-5, 9-10, 12, 14, 19, 21 and 25-26 are canceled. Applicants respectfully urge rejoinder of groups 3 (in part, directed to claims 59-60), and particularly groups 6-8, 11, 13, 15-18, 20, and 22-24 into a single restriction group.

Applicants further amend the method of claim 49 so as to cancel groups 27-28, 32-33 and 36, and respectfully urge rejoinder of groups 29-31, 34-35 and 37-44, either to each other, or to corresponding groups of composition and kit claims. Further, upon entry of the present amendment, Applicants cancel groups 50-76, and reserve the right to prosecute claims directed to the subject matter of any of the claims canceled herein, in this application or in another application sharing the same priority data as the present application.

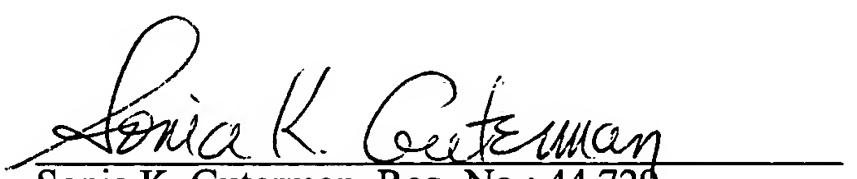
In the present application, the scope and content of several of the groups of claims as here amended are directed to compositions, and have a scope that is the same or substantially the same as that of other claims directed to composition, and the same or similar to claims directed to corresponding method and kit claims that share this same composition or compositions.

Conclusion

In summary, Applicants believe that the claims as here amended are in condition for allowance, which is respectfully requested.

Should questions arise concerning election or reasons for traversal, Applicants invite and encourage the Examiner to contact Applicants' representative at the telephone number below. Applicants respectfully request a month's extension of time for which a petition is hereby made, and enclose a check in the amount of $55.00 for the fee for this extension.

Respectfully submitted,



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